

Cancer patients: Caution against antioxidant supplements

Richard Béliveau

Translated from Le Journal de Montréal, August 27th, 2018

A study has shown that cancer cells use a receptor normally involved in pain signaling to create an antioxidant shield which allows them to withstand free radicals and thus supports the cancer's progress.

RESISTANCE AGAINST FREE RADICALS

Most cancers are caused by a combination of mutations in certain key genes (oncogenes, tumor suppressors and genes involved in DNA repair) which enable these cells to avoid the natural defense systems against cancer and to grow in an abnormal fashion. However, this uncontrolled growth also generates large quantities of free radicals and the tumor cells must therefore, in parallel, develop antioxidant defenses to prevent having the free radicals attack their macromolecular components (DNA, proteins) and cause their death. This antioxidant shield is even more important under certain conditions associated with the development of cancer (inflammation in particular), which themselves also generate large quantities of free radicals and thus create additional oxidative stress in the environment of the cancer cells. The importance of these antioxidant defenses is such that, during tumor progression, there is a strong evolutionary pressure towards selecting the cells which exhibit resistance to oxidative stress.

THE WASABI RECEPTOR TO THE RESCUE

A study which recently appeared in the prestigious journal *Cancer Cell* allows us to appreciate the incredible adaptive abilities used by cancer cells to develop this resistance to free radicals¹. By comparing the genes expressed in normal and cancer cells, a team of researchers from Harvard University observed a strong increase in expression of the gene TRPA1, a receptor normally found at the surface of sensory neurons, whose function is to generate a pain signal in response to allyl isothiocyanate, a molecule present in large quantities in certain members of the mustard family (horseradish and wasabi). The binding of this molecule to TRPA1 is responsible for the burning sensation felt by the nasal lining following excessive ingestion of these condiments.

The surprising presence of a pain receptor at the surface of cancer cells, particularly for cancers of the lung and breast, is not simply random chance. Thanks to a series of elegant experiments, the scientists were able to observe that the activation of TRPA1 generated a flux of calcium into the cells which activated survival pathways that allowed the cells to resist the presence of free radicals. This phenomenon seems to be very important for tumor progression because adding molecules which block the receptor drastically reduced the growth of tumors and also improved the response of these tumors to chemotherapy treatments. In addition, analysis of the expression levels of TRPA1 in biopsies taken from patients with breast or lung cancer showed an association between elevated levels of this protein and decreased survival. Overall,



these observations indicate that the resistance to free radicals obtained by overexpression of TRPA1 is indispensable for tumor progression and could thus represent an interesting target for the development of new anticancer medications.

NO SUPPLEMENTS

The importance of antioxidant defenses for the progression of cancer means that the use of antioxidant supplements for preventing or treating cancer is quite pointless. Far from being useful, these massive doses of antioxidants can actually promote the development of cancer by providing an additional line of defense for the cancer cells. Not to mention that free radicals are required by the immune system to eliminate cancer cells and that the presence of antioxidants is likely to interfere in this process. This is particularly true for patients who have cancer and are being treated with chemotherapy or radiotherapy, because it is the free radicals generated by these treatments which cause reduction in the tumor mass. It should also be noted that the tumors which show the greatest resistance to these treatments are often those which have the highest levels of antioxidant defenses². In addition, some studies have shown that taking antioxidant supplements during and after radiotherapy treatment reduced the effectiveness of the irradiation and significantly increased the risk of recurrence³. Antioxidant supplements are thus products which lack any real use and whose use is strongly discouraged, particularly with regards to prevention or treatment of cancer.

- (1) Takahashi N et al. Cancer cells co-opt the neuronal redox-sensing channel TRPA1 to promote oxidative-stress tolerance. *Cancer Cell* 2018; 33: 985-1003.
- (2) Watson J. Oxidants, antioxidants and the current incurability of metastatic cancers. *Open Biol.* 2013; 3: 120-144.
- (3) Bairati I et al. Randomized trial of antioxidant vitamins to prevent acute adverse effects of radiation therapy in head and neck cancer patients. *J. Clin. Oncol.* 2005; 23:5805-5813.